Practitioner's Docket No. 785-010930-US(PAR)

CHAPTER II

Preliminary Classification:
Proposed Class:
Subclass:

NOTE. "All applicants are requested to include a preliminary classification on newly filed patent applications. The preliminary classification, preferably class and subclass designations, should be identified in the upper right-hand corner of the letter of transmittal accompanying the application papers, for example 'Proposed Class 2, subclass 129.'" M.P.E.P., § 601, 7th ed.

TRANSMITTAL LETTER TO THE UNITED STATES ELECTED OFFICE (EO/US) (ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/09272	22 September 2000	5 October 1999

TITLE OF INVENTION

Method And Device For Moving And Placing Liquid Drops In A Controlled Manner

APPLICANT(S)

Karsten REIHS, Burkhard KOHLER, Dieter RUHLE

Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231
ATTENTION: EO/US

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10*
(When using Express Mail, the Express Mail label number is mandatory; Express Mail certification is optional.)

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☒ deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

37 C.F.R. § 1.8(a)

☐ with sufficient postage as first class mail.

37 C.F.R. § 1.10 *

☒ as "Express Mail Post Office to Addressee" Mailing Label No. EL627432774US **(mandatory)**

TRANSMISSION

☐ facsimile transmitted to the Patent and Trademark Office, (703) _____

Debra G. Conrad
Signature

Date: April 5, 2002

Debra G. Conrad
(type or print name of person certifying)

** Only the date of filing (§ 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under § 1.8 continues to be taken into account in determining timeliness. See § 1.703(f). Consider "Express Mail Post Office to Addressee" (§ 1.10) or facsimile transmission (§ 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.*

NOTE: To avoid abandonment of the application, the applicant shall furnish to the USPTO, not later than 20 months from the priority date: (1) a copy of the international application, unless it has been previously communicated by the International Bureau or unless it was originally filed in the USPTO; and (2) the basic national fee (see 37 C.F.R. § 1.492(a)). The 30-month time limit may not be extended. 37 C.F.R. § 1.495.

***WARNING:** Where the items are those which can be submitted to complete the entry of the international application into the national phase are subsequent to 30 months from the priority date the application is still considered to be in the international state and if mailing procedures are utilized to obtain a date the express mail procedure of 37 C.F.R. § 1.10 must be used (since international application papers are not covered by an ordinary certificate of mailing—See 37 C.F.R. § 1.8.*

NOTE: Documents and fees must be clearly identified as a submission to enter the national state under 35 U.S.C. § 371 otherwise the submission will be considered as being made under 35 U.S.C. § 111. 37 C.F.R. § 1.494(f).

I. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. § 371:

a. ☒ This express request to immediately begin national examination procedures (35 U.S.C. § 371(f)).

b. ☒ The U.S. National Fee (35 U.S.C. § 371(c)(1)) and other fees (37 C.F.R. § 1.492) as indicated below:

2. Fees

JC13 Rec'd PCT/PTO 05 APR 2002

CLAIMS FEE	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
☐*	TOTAL CLAIMS 13	13 −20=	0	× $18.00=	$ 0
	INDEPENDENT CLAIMS 2	2 −3=	0	× $84.00 =	0
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+$ 280.00 =	
BASIC FEE**	☐ U.S. PTO WAS INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where an international preliminary examination fee as set forth in § 1.482 has been paid on the international application to the U.S. PTO: ☐ and the international preliminary examination report states that the criteria of novelty, inventive step (non-obviousness) and industrial activity, as defined in PCT Article 33(1) to (4) have been satisfied for all the claims presented in the application entering the national stage (37 C.F.R. § 1.492(a)(4)) ..... $100.00 ☐ and the above requirements are not met (37 C.F.R. § 1.492(a)(1)) .....$ 710.00 ☒ U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in § 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in § 1.445(a)(2) to the U.S. PTO: ☐ has been paid (37 C.F.R. § 1.492(a)(2)) .....$ 740.00 ☐ has not been paid (37 C.F.R. § 1.492(a)(3)) ..$1,040.00 ☒ where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 C.F.R. § 1.492(a)(5)) ..... $ 890.00				890.00
	Total of above Calculations				= 890.00
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable. Assertion must be made. (note 37 C.F.R. § 1.27)				−
	Subtotal				
	Total National Fee				$ 890.00
	Fee for recording the enclosed assignment document $40.00 (37 C.F.R. § 1.21(h)). (See Item 13 below). See attached "ASSIGNMENT COVER SHEET".				
TOTAL	Total Fees enclosed				$ 890.00

*See attached Preliminary Amendment Reducing the Number of Claims.

☒ Attached is a ☒ check ☐ money order in the amount of $ 890.00

☐ Authorization is hereby made to charge the amount of $ _____

☒ to Deposit Account No. 16-1350

☐ to Credit card as shown on the attached credit card information authorization form PTO-2038.

WARNING: *Credit card information should **not** be included on this form as it may become public.*

☒ Charge any additional fees required by this paper or credit any overpayment in the manner authorized above.

A duplicate of this paper is attached.

**WARNING: *"To avoid abandonment of the application the applicant shall furnish to the United States Patent and Trademark Office not later than the expiration of 30 months from the priority date: * * * (2) the basic national fee (see § 1.492(a)). The 30-month time limit may not be extended." 37 C.F.R. § 1.495(b).*

WARNING: *If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be met within a time period set by the Office. 37 C.F.R. § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40.*

☐ **Assertion of Small Entity Status**

☐ **Applicant hereby asserts status as a small entity under 37 C.F.R. § 1.27.**

NOTE: 37 C.F.R. § 1.27(c) deals with the assertion of small entity status, whether by a written specific declaration thereof or by payment as a small entity of the basic filing fee or the fee for the entry into the national phase as states:

"(c) Assertion of small entity status. Any party (person, small business concern or nonprofit organization) should make a determination, pursuant to paragraph (f) of this section, of entitlement to be accorded small entity status based on the definitions set forth in paragraph (a) of this section, and must, in order to establish small entity status for the purpose of paying small entity fees, actually make an assertion of entitlement to small entity status, in the manner set forth in paragraphs (c)(1) or (c)(3) of this section, in the application or patent in which such small entity fees are to be paid.

(1) Assertion by writing. Small entity status may be established by a written assertion of entitlement to small entity status. A written assertion must:

(i) Be clearly identifiable;

(ii) Be signed (see paragraph (c)(2) of this section); and

(iii) Convey the concept of entitlement to small entity status, such as by stating that applicant is a small entity, or that small entity status is entitled to be asserted for the application or patent. While no specific words or wording are required to assert small entity status, the intent to assert small entity status must be clearly indicated in order to comply with the assertion requirement.

(2) Parties who can sign and file the written assertion. The written assertion can be signed by:

(i) One of the parties identified in §§ 1.33(b) (e.g., an attorney or agent registered with the Office), §§ 3.73(b) of this chapter notwithstanding, who can also file the written assertion;

(ii) At least one of the individuals identified as an inventor (even though a §§ 1.63 executed oath or declaration has not been submitted), notwithstanding §§ 1.33(b)(4), who can also file the written assertion pursuant to the exception under §§ 1.33(b) of this part; or

(iii) An assignee of an undivided part interest, notwithstanding §§ 1.33(b)(3) and 3.73(b) of this chapter, but the partial assignee cannot file the assertion without resort to a party identified under §§ 1.33(b) of this part.

(3) Assertion by payment of the small entity basic filing or basic national fee. The payment, by any party, of the exact amount of one of the small entity basic filing fees set forth in §§ 1.16(a), (f), (g), (h), or (k), or one of the small entity basic national fees set forth in §§ 1.492(a)(1), (a)(2), (a)(3), (a)(4), or (a)(5), will be treated as a written assertion of entitlement to small entity status even if the type of basic filing or basic national fee is inadvertently selected in error.

(i) If the Office accords small entity status based on payment of a small entity basic filing or basic national fee under paragraph (c)(3) of this section that is not applicable to that application, any balance of the small entity fee that is applicable to that application will be due along with the appropriate surcharge set forth in §§ 1.16(e), or §§ 1.16(l).

(ii) The payment of any small entity fee other than those set forth in paragraph (c)(3) of this section (whether in the exact fee amount or not) will not be treated as a written assertion of entitlement to small entity status and will not be sufficient to establish small entity status in an application or a patent."

3. ☒ A copy of the International application as filed (35 U.S.C. § 371(c)(2)):

NOTE: *Section 1.495 (b) was amended to require that the basic national fee and a copy of the international application must be filed with the Office by 30 months from the priority date to avoid abandonment. "The International Bureau normally provides the copy of the international application to the Office in accordance with PCT Article 20. At the same time, the International Bureau notifies applicant of the communication to the Office. In accordance with PCT Rule 47.1, that notice shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place. Thus, if the applicant desires to enter the national stage, the applicant normally need only check to be sure the notice from the International Bureau has been received and then pay the basic national fee by 30 months from the priority date." Notice of Jan. 7, 1993, 1147 O.G. 29 to 40, at 35-36. See item 14c below.*

a. ☐ is transmitted herewith.

b. ☐ is not required, as the application was filed with the United States Receiving Office.

c. ☒ has been transmitted

i. ☒ by the International Bureau.

Date of mailing of the application (from form PCT/1B/308): 4/12/01.

ii. ☐ by applicant on _____. *(Date)*

4. ☒ A translation of the International application into the English language (35 U.S.C. § 371(c)(2)):

a. ☒ is transmitted herewith.

b. ☐ is not required as the application was filed in English.

c. ☐ was previously transmitted by applicant on _____. *(Date)*

d. ☐ will follow.

5. ☒ Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. § 371(c)(3)):

NOTE: The Notice of January 7, 1993 points out that 37 C.F.R. § 1.495(a) was amended to clarify the existing and continuing practice that PCT Article 19 amendments must be submitted by 30 months from the priority date and this deadline may not be extended. The Notice further advises that: "The failure to do so will not result in loss of the subject matter of the PCT Article 19 amendments. Applicant may submit that subject matter in a preliminary amendment filed under section 1.121. In many cases, filing an amendment under section 1.121 is preferable since grammatical or idiomatic errors may be corrected." 1147 O.G. 29-40, at 36.

a. ☐ are transmitted herewith.

b. ☐ have been transmitted

i. ☐ by the International Bureau.

Date of mailing of the amendment (from form PCT/1B/308):

_____.

ii. ☐ by applicant on _____. *(Date)*

c. ☒ have not been transmitted as

i. ☒ applicant chose not to make amendments under PCT Article 19. Date of mailing of Search Report (from form PCT/ISA/210.):

1/3/01.

ii. ☐ the time limit for the submission of amendments has not yet expired. The amendments or a statement that amendments have not been made will be transmitted before the expiration of the time limit under PCT Rule 46.1.

6. ☒ A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. § 371(c)(3)):

a. ☐ is transmitted herewith.

b. ☐ is not required as the amendments were made in the English language.

c. ☒ has not been transmitted for reasons indicated at point 5(c) above.

7. ☒ A copy of the international examination report (PCT/IPEA/409)

☒ is transmitted herewith.

☐ is not required as the application was filed with the United States Receiving Office.

8. ☐ Annex(es) to the international preliminary examination report

a. ☐ is/are transmitted herewith.

b. ☐ is/are not required as the application was filed with the United States Receiving Office.

9. ☐ A translation of the annexes to the international preliminary examination report

a. ☐ is transmitted herewith.

b. ☐ is not required as the annexes are in the English language.

10. ☒ An oath or declaration of the inventor (35 U.S.C. § 371(c)(4)) complying with 35 U.S.C. § 115

a. ☐ was previously submitted by applicant on _____. *(Date)*

b. ☐ is submitted herewith, and such oath or declaration

i. ☐ is attached to the application.

ii. ☐ identifies the application and any amendments under PCT Article 19 that were transmitted as stated in points 3(b) or 3(c) and 5(b); and states that they were reviewed by the inventor as required by 37 C.F.R. § 1.70.

c. ☒ will follow.

II. Other document(s) or information included:

11. ☒ An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a):

a. ☒ is transmitted herewith.

b. ☐ has been transmitted by the International Bureau.

Date of mailing (from form PCT/IB/308): _____.

c. ☐ is not required, as the application was searched by the United States International Searching Authority.

d. ☐ will be transmitted promptly upon request.

e. ☐ has been submitted by applicant on _____. *(Date)*

12. ☒ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98:

a. ☐ is transmitted herewith.

Also transmitted herewith is/are:

☐ Form PTO-1449 (PTO/SB/08A and 08B).

☐ Copies of citations listed.

b. ☒ will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. § 371(c).

c. ☐ was previously submitted by applicant on _____. *(Date)*

13. ☐ An assignment document is transmitted herewith for recording.

A separate ☐ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

_____

_____

_____

14. ☒ Additional documents:
    a. ☐ Copy of request (PCT/RO/101)
    b. ☒ International Publication No. WO 01/24934 A1
        i. ☐ Specification, claims and drawing
        ii. ☒ Front page only
    c. ☒ Preliminary amendment (37 C.F.R. § 1.121)
    d. ☒ Other
    PCT/IB/308, PCT/IB/306

15. ☒ The above checked items are being transmitted
    a. ☒ before 30 months from any claimed priority date.
    b. ☐ after 30 months.

16. ☐ Certain requirements under 35 U.S.C. § 371 were previously submitted by the applicant on _____, namely:

AUTHORIZATION TO CHARGE ADDITIONAL FEES

WARNING: *Accurately count claims, especially multiple dependant claims, to avoid unexpected high charges if extra claims are authorized.*

NOTE: "A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission." 37 C.F.R. § 1.136(a)(3).

NOTE: "Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account." 37 C.F.R. § 1.26(a).

☒ Please charge, in the manner authorized above, the following additional fees that may be required by this paper and during the entire pendency of this application:

☒ 37 C.F.R. § 1.492(a)(1), (2), (3), and (4) (filing fees)

WARNING: *Because failure to pay the national fee within 30 months without extension (37 C.F.R. § 1.495(b)(2)) results in abandonment of the application, it would be best to always check the above box.*

☒ 37 C.F.R. § 1.492(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 C.F.R. § 1.492(d)), it might be best not to authorize the PTO to charge additional claim fees, except possible when dealing with amendments after final action.

☒ 37 C.F.R. § 1.17 (application processing fees)

☒ 37 C.F.R. § 1.17(a)(1)–(5) (extension fees pursuant to § 1.136(a).

☐ 37 C.F.R. § 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. § 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 C.F.R. § 1.311(b).

NOTE: 37 C.F.R. § 1.28(b) requires "Notification of any change in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying . . . issue fee." From the wording of 37 C.F.R. § 1.28(b): (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

☒ 37 C.F.R. § 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 30 months after the priority date).

SIGNATURE OF PRACTITIONER

Reg. No.: 24,622

Clarence A. Green

(type or print name of practitioner)

Tel. No.: (203) 259-1800

PERMAN & GREEN, LLP

P.O. Address

Customer No.: 2512

425 Post Road, Fairfield, CT 06430 USA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

EXPRESS MAIL NO.:EL627432774US
APPLICANT(S): REIHS et al.
INTERNATIONAL APPLICATION NO.: PCT/EP00/09272
INTERNATIONAL FILING DATE: 9/22/00
TITLE: METHOD AND DEVICE FOR MOVING AND PLACING LIQUID DROPS IN A CONTROLLED MANNER
ATTORNEY DOCKET NO.: 785-010930-US(PAR)

Box PCT
Commissioner of Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Please amend the above-identified, patent application as follows:

IN THE SPECIFICATION:

After the Title and before the first paragraph, please insert the following new paragraph:

--(New) This application claims the benefit of the earlier filed International Application No. PCT/EP00/09272, International Filing Date, 22 September 2000, which designated the United States of America, and which international application was published under PCT Article 21(2) in German as WO Publication No. WO 01/24934 A1.--

After the Heading "Claims" and before claim 1, please insert the following:

--What is claimed is:--

IN THE CLAIMS

Please amend Claims 3 and 6 through 13 as rewritten below:

3. (Amended) The method according to claim 1, characterized in that a voltage of from 100 to 1000 volts, preferably from 400 to 600 volts, is applied between manipulator (10) and support (7) in order to generate the electric field.

6. (Amended) The device according to claim 1, characterized in that the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function S(log f) = a(f) x f calculated between the integration limits log ($f_1/\mu m^{-1}$) = -3 and log ($f_1/\mu m^{-1}$) = 3 is at least 0.5 and consists of ultraphobic polymers or durably ultraphobic materials.

7. (Amended) The device according to claim 1, characterized in that the ultraphobic surface is a structured aluminum surface coated with an ultraphobic material.

8. (Amended) The device according to claim 1, characterized in that the ultraphobic surface is an

aluminum surface treated with steam and coated with an ultraphobic material.

9. (Amended) The device according to claim 1, characterized in that the ultraphobic surface is a surface which is coated with $Ni(OH)_2$ particles and covered with an ultraphobic material.

10. (Amended) The device according to claim 1, characterized in that the ultraphobic surface is a sandblasted surface covered with an ultraphobic material.

11. (Amended) The device according to claim 1, characterized in that the ultraphobic surface is a tungsten carbide surface structured by a laser and covered with an ultraphobic material.

12. (Amended) Use of the device according to claim 4 in the dosage of liquids on a microscopic scale, especially in a range of from 10^{-5} to 10^{-12} liters, preferably from 10^{-9} to 10^{-6} liters.

13. (Amended) Use of the device according to claim 4 in biochemical or chemical processes, preferably in PCR, ELISA and/or in the determination of enzyme activity.

REMARKS

In accordance with 37 C.F.R. §1.121 (as amended on 11/7/2000) the rewritten claim(s) above are shown on

separate page(s) marked up to show all the changes relative to the previous version of that section.

Respectfully submitted,

5 April 02

Clarence A. Green Reg. No.: 24,622
PERMAN & GREEN, LLP
425 Post Road, Fairfield, CT 06430
(203) 259-1800
Customer No.: 2512

Date

Application entitled: METHOD AND DEVICE FOR MOVING AND PLACING LIQUID DROPS IN A CONTROLLED MANNER

MARKED UP CLAIMS:

3. (Amended) The method according to claim 1 ~~or 2~~, characterized in that a voltage of from 100 to 1000 volts, preferably from 400 to 600 volts, is applied between manipulator (10) and support (7) in order to generate the electric field.

6. (Amended) The device according to ~~any of claims~~claim 1 ~~to 5~~, characterized in that the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function S(log f) = a(f) x f calculated between the integration limits log $(f_1/\mu m^{-1})$ = -3 and log $(f_1/\mu m^{-1})$ = 3 is at least 0.5 ultraphobic materials.

7. (Amended) The device according to ~~any of claims~~claim 1 ~~to 6~~, characterized in that the ultraphobic surface is a structured aluminum surface coated with an ultraphobic material.

8. (Amended) The device according to ~~any of claims~~claim 1 ~~to 6~~, characterized in that the ultraphobic surface is an aluminum surface treated with steam and coated with an ultraphobic material.

9. (Amended) The device according to ~~any of claims~~claim 1 ~~to 6~~, characterized in that the ul-

traphobic surface is a surface which is coated with $Ni(OH)_2$ particles and covered with an ultraphobic material.

10. (Amended) The device according to ~~any of claims~~claim 1 ~~to 6~~, characterized in that the ultraphobic surface is a sandblasted surface covered with an ultraphobic material.

11. (Amended) The device according to ~~any of claims~~claim 1 ~~to 6~~, characterized in that the ultraphobic surface is a tungsten carbide surface structured by a laser and covered with an ultraphobic material.

12. (Amended) Use of the device according to ~~any of claims~~claim 4 ~~to 11~~ in the dosage of liquids on a microscopic scale, especially in a range of from 10^{-5} to 10^{-12} liters, preferably from 10^{-9} to 10^{-6} liters.

13. (Amended) Use of the device according to ~~any of claims~~claim 4 ~~to 11~~ in biochemical or chemical processes, preferably in PCR, ELISA and/or in the determination of enzyme activity.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

EXPRESS MAIL NO.: EL627434302US
APPLICANT(S):REIHS et al.
INTERNATIONAL APPLICATION NO.: PCT/EP00/09272
INTERNATIONAL FILING DATE: 9/22/00
U.S. SERIAL NUMBER: 10/089,933
TITLE: METHOD AND DEVICE FOR MOVING AND PLACING LIQUID DROPS IN A CONTROLLED MANNER
ATTORNEY DOCKET NO.: 785-010930-US(PAR)

Box PCT
Commissioner of Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Please amend the above-identified, patent application as follows:

IN THE SPECIFICATION:

Please delete paragraph 6 on page 3 and replace with the following replacement paragraph:

-- In a preferred embodiment, the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function S(log f)=a(f) x f calculated between the

integration limits $\log(f_1/\mu m^{-1}) = -3$ and $\log (f_1/\mu m^{-1}) = 3$ is at least 0.5 and consists of a hygrophobic or, in particular, oleophobic material, or of a durably hydrophobized or, in particular, durably oleophobized material. Such an ultraphobic surface has been described in the International Patent Publication No. WO 00/39240.--

Please delete paragraph 3 on page 4, and replace with the following replacement paragraph:

--The ultraphobic surface preferably is an aluminum surface which is provided with microstrutures, anodized, optionally sealed, calcined, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Publication No. WO 00/39369.--

Please delete paragraph 5 on page 4, and replace with the following replacement paragraph:

--It is also preferred that the ultraphobic surface be an aluminum surface which optionally is anodically oxidized, sealed with hot water or steam, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Publication No. WO 00/39368. The dosing tip can be made entirely of aluminum or preferably has an aluminum coating, the aluminum being treated as stated above.--

Please delete paragraph 6 on page 4, and replace with the following replacement paragraph:

--Furthermore, the ultraphobic surface preferably is a surface which is coated with $Ni(OH)_2$ particles, optionally coated with an adhesion promoter, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Publication No. WO 00/39239. The $Ni(OH)_2$ particles preferably have a diameter d_{50} of from 0.5 to 20 µm.--

Please delete paragraph 1 on page 5, and replace with the following replacement paragraph:

--In another advantageous embodiment, the ultraphobic surface is made of tungsten carbide which is structured with a laser, optionally coated with an adhesion promoter, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Publication No. WO 00/39051. Preferably, the dosing tip is coated with tungsten carbide only, which then is treated as stated above. The tungsten carbide preferably has a layer thickness of from 10 to 500 µm.--

Please delete paragraph 2 on page 5, and replace with the following replacement paragraph:

--Furthermore, the surface preferably is sandblasted using a blasting means, optionally coated with an adhesion-promoting layer, and subsequently provided

with a hydrophobic and/or oleophobic coating as described in the International Patent Publication No. WO 00/38845.--

A marked-up version of the rewritten paragraphs is attached hereto.

IN THE CLAIMS:

Please cancel Claims 1 through 13 without prejudice.

Please add the following new claims 14 through 36 as written below:

14. (New) A substrate in which several electrodes are placed on which varying voltages can be applied individually and said substrate being provided with an ultraphobic surface.

15. (New) The substrate according to claim 14, wherein the electrodes are substantially aligned with the surface of the substrate.

16. (New) The substrate according to claim 15, wherein the electrodes are aligned at a constant screen.

17. (New) A device for dosing liquid drops which device has at least one support, an electrically chargeable manipulator and a means for generating an inhomogeneous electric field.

18. (New) The substrate according to claim 14, wherein the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function S(log(f))=a(f)xf calculated between the integration limits $\log(f_1/\mu m^{-1})=-3$ and $\log(f_1/\mu m^{-1})=3$ is at least 0.3 and consists of ultraphobic polymers or durably ultraphobic materials.

19. (New) The substrate according to claim 14, wherein the ultraphobic surface is a structured aluminum surface coated with a hydrophobic and/or oleophobic material.

20. (New) The substrate according to claim 14, wherein the ultraphobic surface is an aluminum surface treated with steam and coated with a hydrophobic and/or oleophobic material.

21. (New) The substrate according to claim 14, wherein the ultraphobic surface is a surface which is coated with $Ni(OH)_2$ particles and covered with a hydrophobic and/or oleophobic material.

22. (New) The substrate according to claim 14, wherein the ultraphobic surface is a sandblasted surface covered with a hydrophobic and/or oleophobic material.

23. (New) The substrate according to claim 14, wherein the ultraphobic surface is a tungsten carbide

surface structured by a laser and covered with a hydrophobic and/or oleophobic material.

24. (New) A method of moving or dosing liquid drops on a microscopic scale, wherein the liquid drops are moved on a support having an ultraphobic surface, using an inhomogeneous electric field.

25. (New) The method according to claim 24, wherein the electric field is generated by several electrodes on which varying voltages can be applied individually and which are aligned at a constant screen.

26. (New) The method according to claim 25, wherein inside the screen of electrodes a liquid drop is moveable in any direction.

27. (New) The method according to claim 25, wherein several liquid drops are moved and combined inside the screen of electrodes.

28. (New) A method according to claim 24, wherein the liquid drops are in the range of from about 10^{-9} to about 10^{-12} liters.

29. (New) A device according to claim 17, wherein the device is adapted for dosing liquid drops on a microscopic scale in a range of from about 10^{-9} to about 10^{-12} liters.

30. (New) The substrate according to claim 14, wherein the substrate is adapted for moving liquid drops on a microscopic scale in a range of from about 10^{-9} to about 10^{-12} liters.

31. (New) A method for performing a chemical or biochemical process comprising the steps of:

moving or dosing liquid drops in accordance with the method as in claim 24; and

using the liquid drops in at least one of a polymerase chain reaction, enzyme-linked immunosorbent assay or a determination of enzyme activity.

32. (New) The device according to claim 17, wherein the device doses liquid drops for at least one of a polymerase chain reaction, enzyme-linked immunosorbent assay or a determination of enzyme activity.

33. (New) The substrate according to claim 14, wherein the substrate is adapted for effecting at least in part at least one of a polymerase chain reaction, enzyme-linked immunosorbent assay or a determination of enzyme activity.

34. (New) A method of producing a substrate according to claim 14, wherein the electrodes are placed in the substrate and the surface of the substrate is coated with an ultraphobic layer.

35. (New) The method according to claim 34, wherein the electrodes are placed substantially aligned with the surface of the substrate.

36. (New) The method according to claim 34, wherein the electrodes are placed in the substrate at a constant screen.

Respectfully submitted,

8/12/02

Date

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Application entitled: TITLE: METHOD AND DEVICE FOR MOVING AND PLACING LIQUID DROPS IN A CONTROLLED MANNER
US Serial No.: 10/089,933

Marked Up Specification Replacement Paragraph(s)

Page 3, paragraph 6:

In a preferred embodiment, the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function S(log f)=a(f) x f calculated between the integration limits $\log(f_1/\mu m^{-1}) = -3$ and $\log (f_1/\mu m^{-1}) = 3$ is at least 0.5 and consists of a hygrophobic or, in particular, oleophobic material, or of a durably hydrophobized or, in particular, durably oleophobized material. Such an ultraphobic surface has been described in the International Patent ~~Application WO 99/10322~~Publication No. WO 00/39240.

Page 4, paragraph 3:

The ultraphobic surface preferably is an aluminum surface which is provided with microstrutures, anodized, optionally sealed, calcined, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent ~~Application WO 99/10323~~Publication No. WO 00/39369.

Page 4, paragraph 5:

It is also preferred that the ultraphobic surface be an aluminum surface which optionally is anodically oxidized, sealed with hot water or steam, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent ~~Application 99/10324~~Publication No. WO 00/39368. The dosing tip can be made entirely of aluminum or preferably has an aluminum coating, the aluminum being treated as stated above.

Page 4, paragraph 6:

Furthermore, the ultraphobic surface preferably is a surface which is coated with $Ni(OH)_2$ particles, optionally coated with an adhesion promoter, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent ~~Application WO 99/10111~~Publication No. WO 00/39239. The $Ni(OH)_2$ particles preferably have a diameter d_{50} of from 0.5 to 20 µm.

Page 5, paragraph 1:

In another advantageous embodiment, the ultraphobic surface is made of tungsten carbide which is structured with a laser, optionally coated with an adhesion promoter, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent ~~Application WO 99/10113~~Publication No. WO 00/39051. Preferably, the dosing tip is coated with tungsten carbide only, which

then is treated as stated above. The tungsten carbide preferably has a layer thickness of from 10 to 500 µm.

Page 5, paragraph 2:

Furthermore, the surface preferably is sandblasted using a blasting means, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent ~~Application WO 99/10112~~Publication No. WO 00/38845.

4/prts

METHOD AND DEVICE FOR MOVING AND PLACING LIQUID DROPS IN A CONTROLLED MANNER

The present invention relates to a method and a device for moving and dosing amounts of liquid on a microscopic scale with a volume of especially 10^{-12} to 10^{-6} liters by means of an electric field using a support with an ultraphobic surface, optionally in association with an ultraphobic dosing tip.

Manipulating and, in particular, dosing of extremely small drops of liquid having a volume in the order of 10^{-12} - 10^{-6} liters or a diameter in the order of about 0.01 - 1 mm represents a problem even today, because even an extremely small loss of liquid during this process, also referred to as microdosing, will give rise to substantial deviations from the desired dosage quantity. Such loss of liquid arises if e.g. the drop of liquid is shifted along a conventional surface, because part of the liquid drop will adhere to the surface even in the event of a highly smooth surface.

The object is therefore to provide a method of moving and dosing liquid drops having a volume of especially less than 10^{-6} liters without significant loss of liquid.

According to the invention, said object is accomplished by providing a method of microdosing liquid drops, wherein the liquid drops are moved free of loss by means of an inhomogeneous electric field on a support having an ultraphobic surface.

The invention is directed to a method of moving or dosing liquid drops on a microscopic scale, which method is characterized in that the liquid drops are moved on a support having an ultraphobic surface, using an inhomogeneous electric field, preferably an inhomogeneous field between said support and a manipulator.

Preferably, an electrically charged tip or wire, particularly a tip or wire having an ultraphobic surface is used as manipulator.

In a preferred embodiment, a voltage of from 100 to 1000 volts, preferably from 400 to 600 volts, is applied between manipulator and support in order to generate the electric field. Depending on the geometry of the array, the voltage may vary within a wide range.

The invention is also directed to a device for the microdosage of liquid drops, which device has at least one support having an ultraphobic surface, optionally at least one liquid reservoir, an electrically chargeable manipulator, and a means for generating an inhomogeneous electric field. Optionally, said manipulator can also be an ultraphobic tip/wire or the like.

A liquid drop in the meaning of the invention may consist of any liquid and preferably has a volume of from 10^{-12} to 10^{-6} liters, more preferably from 10^{-9} to 10^{-6} liters. According to the invention, such a drop is shifted without loss on an ultraphobic surface, using a shiftable electric field.

It is also preferred to separate a liquid drop from a liquid reservoir by means of the electric field. Using the electric field, it is possible to combine and thereby mix a plurality of liquid drops on an ultraphobic surface. All of these process steps can also be performed in any combination of each other.

In a preferred embodiment, the electric field is present between a tip, which tip preferably has a diameter of from 0.01 to 1 mm, any desired length and an ultraphobic surface, and a preferably metallic support. Using said tip, liquid drops are shifted on the ultraphobic surface. The tip has an ultraphobic surface, which is why there is no adhering of liquid particles to the tip.

The liquid drops assume a nearly spherical shape both at the tip and on the ultraphobic surface and therefore, the volumes thereof can be calculated easily from the diameter determined e.g. under a microscope.

In another preferred embodiment, the liquid reservoir of the device has an electrostatic charging means.

Ultraphobic surfaces in the meaning of the invention involve the feature that the contact angle of a water drop resting on the surface is more than 150° and the roll-off angle is not more than 10°.

The roll-off angle is understood to be the angle of inclination of a basically planar, yet structured surface relative to the horizontal line, at which angle a resting drop of water 10 µl in volume is moved due to gravity when tilting the surface.

For example, such ultraphobic surfaces have been disclosed in the laid-open documents WO 98/23549, WO 96/04123, WO 96/21523, and WO 96/34697, which hereby are incorporated by reference and thus deemed to be part of the disclosure.

In a preferred embodiment, the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function $S(\log f) = a(f) \times f$ calculated between the integration limits $\log(f_1/\mu m^{-1}) = -3$ and $\log(f_1/\mu m^{-1}) = 3$ is at least 0.5 and consists of a hydrophobic or, in particular, oleophobic material, or of a durably hydrophobized or, in particular, durably oleophobized material. Such an ultraphobic surface has been described in the International Patent Application WO 99/10322.

In the meaning of the invention, a hydrophobic material is a material which exhibits a contact angle, related to water, of more than 90° on a planar, non-structured surface.

In the meaning of the invention, an oleophobic material is a material which exhibits a contact angle, related to long-chain n-alkanes such as n-decane, of more than 90° on a planar, non-structured surface.

The ultraphobic surface preferably is an aluminum surface which is provided with microstructures, anodized, optionally sealed, calcined, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Application WO 99/10323.

The manipulator and/or support can be made entirely of aluminum or preferably has an aluminum coating, the aluminum being treated as stated above.

It is also preferred that the ultraphobic surface be an aluminum surface which optionally is anodically oxidized, sealed with hot water or steam, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Application 99/10324. The dosing tip can be made entirely of aluminum or preferably has an aluminum coating, the aluminum being treated as stated above.

Furthermore, the ultraphobic surface preferably is a surface which is coated with $Ni(OH)_2$ particles, optionally coated with an adhesion promoter, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Application WO 99/10111. The $Ni(OH)_2$ particles preferably have a diameter d_{50} of from 0.5 to 20 μm.

In another advantageous embodiment, the ultraphobic surface is made of tungsten carbide which is structured with a laser, optionally coated with an adhesion promoter, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Application WO 99/10113. Preferably, the dosing tip is coated with tungsten carbide only, which then is treated as stated above. The tungsten carbide preferably has a layer thickness of from 10 to 500 μm.

Furthermore, the surface preferably is sandblasted using a blasting means, optionally coated with an adhesion-promoting layer, and subsequently provided with a hydrophobic and/or oleophobic coating as described in the International Patent Application WO 99/10112.

Any surface-active phobizing aid of any molar mass is suitable as hydrophobic and/or oleophobic coating of the above-mentioned surfaces. These compounds are cationic, anionic, amphoteric and/or non-ionic surface-active compounds as listed in the index "Surfactants Europe, A Dictionary of Surface-Active Agents Available in Europe, Edited by Gordon L. Hollis, Royal Society of Chemistry, Cambridge, 1995.

For example, the following may be mentioned as anionic phobizing aids: alkyl sulfates, ether sulfates, ether carboxylates, phosphate esters, sulfosuccinates, sulfosuccinate amides, paraffin sulfonates, olefin sulfonates, sarcosinates, isothionates, taurates, and lignin compounds.

For example, quaternary alkylammonium compounds and imidazoles may be mentioned as cationic phobizing aids.

Amphoteric phobizing aids are betaines, glycinates, propionates, and imidazoles, for example.

Non-ionic phobizing aids are e.g. alkoxylates, alkylamides, esters, amine oxides, and alkylpolyglycosides. Furthermore, reaction products of alkylene oxides with alkylatable compounds such as fatty alcohols, fatty amines, fatty acids, phenols, alkylphenols, arylalkylphenols such as styrene-phenol condensation products, carboxylic acid amides, and rosin acids are possible.

Those phobizing aids are particularly preferred wherein from 1 to 100%, more preferably from 60 to 95% of the hydrogen atoms are substituted by fluorine atoms. Perfluorinated alkyl sulfates, perfluorinated alkyl sulfonates, perfluorinated alkyl phosphonates, perfluorinated alkyl phosphinates, and perfluorinated carboxylic acids may be mentioned as examples.

Preferably, compounds having a molar mass m.w. > 500 - 1,000,000, preferably 1,000 - 500,000, and more preferably 1,500 - 20,000 are employed as polymeric phobizing aids in hydrophobic coating, or as polymeric hydrophobic material for the surface. These polymer phobizing aids can be non-ionic, anionic, cationic, or amphoteric compounds. Furthermore, these polymer phobizing aids can be homo- and copolymers, graft polymers and graft copolymers, as well as random block polymers.

Particularly preferred polymer phobizing aids are AB, BAB and ABC type block polymers. In AB or BAB block polymers, the A segment is a hydrophilic homopolymer or copolymer, and the B block is a hydrophobic homopolymer or copolymer or a salt thereof.

Also, anionic polymeric phobizing aids, especially condensation products of aromatic sulfonic acids with formaldehyde and alkylnaphthalenesulfonic acids, or of formaldehyde, naphthalenesulfonic acids and/or benzenesulfonic acids, and condensation products of optionally substituted phenol with formaldehyde and sodium bisulfite are particularly preferred.

Also preferred are those condensation products which can be obtained by reaction of naphthols with alkanols, addition of alkylene oxide and at least partial conversion of the terminal hydroxy groups to sulfo groups or semi-esters of maleic acid and phthalic acid or succinic acid.

In another preferred embodiment, the phobizing aid is from the group of sulfosuccinic esters and alkylbenzenesulfonates. Sulfated, alkoxylated fatty acids or salts thereof are also preferred. Alkoxylated fatty alcohols are understood to be C_6-C_{22} fatty alcohols, saturated or unsaturated, particularly stearyl alcohol, provided with 5 to 120, 6 to 60, and in a particularly preferred fashion, with 7 to 30 ethylene oxide units. The sulfated alkoxylated fatty alcohols preferably are present as salts, particularly as alkali or amine salts, preferably as diethylamine salt.

Preferred fields of use for the method and device according to the invention are biochemical or chemical methods wherein microscopic volumes of liquid have to be moved, mixed or dosed. The following may be mentioned as examples: the PCR (polymerase chain reaction), ELISA (enzyme-linked immunosorbent assay), or the determination of enzyme activity.

The method according to the invention is easier to perform compared to conventional microdosing using pressure. As a result of the minimal adhesion of liquid drops to the ultraphobic surfaces, manipulation of extremely small drops of liquid is possible without loss, thereby avoiding dosage errors.

The invention is also directed to the use of the device of the invention in the dosage of liquids on a microscopic scale, especially in a range of from 10^{-6} to 10^{-12} liters.

With reference to the Figures 1 to 4, the device according to the invention will be exemplified in more detail below.

Fig. 1 shows a plastic plate 2 for shifting liquid drops 4, 5 using a plurality of electrodes 3.

Fig. 2 shows as an aluminum plate 7 having an electrically charged tip 10 as manipulator.

Fig. 3 shows a round tip 12 with an annular electrode 13 for discharging small volumes of liquid 15 from a reservoir 14 (cross-sectional drawing).

Fig. 4 shows an array of three tips 16 forming a nearly triangular gap M which can be used instead of annular electrode 13 in Fig. 3 to discharge small amounts of liquid from a reservoir.

Examples

Example 1

Figure 1 shows a device 1 of the invention for shifting liquid drops (in this event: aqueous solutions) on solid surfaces without leaving a residue.

The device consists of a substrate 2 (in this event: plexiglass), the surface of which is provided with round, electrically conductive electrodes 3 (diameter 1 mm, spacing 5 mm) aligned with the surface of the substrate. Varying voltages can be applied at the individual electrodes 3.

The surface of substrate 2 is provided with an electrically insulating ultraphobic coating about 5 μm in thickness. To this end, a layer of aluminum about 5 μm in thickness is vapor-deposited on the substrate. The Al layer is subjected to anodic oxidation, treated with hot steam, and provided with a hydrophobic coating. To produce the hydrophobic coating, the substrate is immersed in a 1 wt.-% so-

lution of Fluowet PL80 from Clariant Company for 5 hours at pH 7, rinsed with water, and dried at 60°C.

Producing the ultrahydrophobic coating:

a. Metallizing:

An aluminum layer about 5 μm in thickness is thermally vapor-deposited on the substrate. The surface is subsequently degreased for 3 minutes in distilled chloroform ($CHCl_3$).

b. Anodic oxidation:

Anodic oxidation of the aluminum surface is performed in 1N sulfuric acid with continuous electrolyte agitation under laminar flow conditions. The electrolyte temperature of 20°C is controlled by a thermostat. The spacing between the substrate material and the counterelectrode made of $AlMg_3$, semi-rigid, is 5 cm. The current density during the anodic oxidation is controlled to be a constant 10 mA/cm^2. The oxidation is continued until an oxide layer about 2-3 μm in thickness is formed.

c. Treatment with water:

Following anodic oxidation, the sample is rinsed in distilled water for 5 minutes and subsequently in methanol for 1 minute. Following drying (air, room temperature), the sample is treated in distilled water at 100°C for 15 minutes in a beaker which previously has been boiled with distilled water several times. This treatment is followed by rinsing in methanol (1 min) and drying at 80°C in a drying oven for 1 hour.

As a result of this treatment, the Al layer is converted completely to an aluminum oxide layer.

Handling of the device:

Initially, all of the electrodes 3 are supplied with the same electric potential. A drop 5 can be shifted towards a directly adjacent electrode by switching this electrode to a potential of 800 V versus the other electrodes. Thereafter, the drop comes to rest above the respective electrode.

By repeated switching of the electrodes 3, the movement of the drop 5 on the surface can be controlled at will within the electrode screen. In this way, different drops 4, 5 can be shifted to the same position and made to combine.

The movement of the drops 4, 5 on the ultraphobic surface proceeds without leaving a residue, i.e., without adherence of liquid residues along the path of movement. This can be established as follows: A drop 4 (about 1 mm in diameter) of a solution of 4-(6-diethylamino-3-diethylimino-3H-xanth-9-yl)-1,3-benzenedisulfonic acid (Kiton Red, concentration: 1×10^{-2} mol/l in water) rests on the ultraphobic surface. The drop 4 is shifted along a closed path via 8 electrodes (length of path: 40 mm). This process is repeated 10 times, so that the overall path is 400 mm. Subsequently, the drop is removed, and a drop of pure water is likewise shifted 10 times along the closed path previously used.

This water drop is subjected to a spectrophotometric investigation. No dye can be detected down to the detection limit of 10^{-10} mol/l (based on drop volume). Hence, losses as a result of shifting the drop are less than 10 ppb.

Correspondingly, the example illustrated above can also be used for liquid drops surrounded by solid walls on all sides, e.g. in gaps or tubes. Consequently, these embodiments permit conveyance of liquids without loss merely by varying electric fields, i.e., without mechanically moving parts.

Example 2

Figure 2 shows a device 6 of the invention for complete transfer of liquid drops (in this event: aqueous solutions) using a movable tip 10.

The device has a support plate 7 of aluminum with an ultraphobic coating and a tip 10. The tip also has an ultraphobic surface. The ultraphobic coating is produced in accordance with Example 1.

Handling of the device:

A drop 8 of a solution of 4-(6-diethylamino-3-diethylimino-3H-xanth-9-yl)-1,3-benzenedisulfonic acid (Kiton Red, concentration: 1×10^{-2} mol/l in water) rests on the ultraphobic surface. The volume $V = (3.00 \pm 0.05) \times 10^{-9}$ liters. The volume has been determined via the diameter of the spherical drop, using a measuring microscope.

The drop 8 can be picked up by means of tip 10. To this end, the tip is approached to a distance of about 5 mm, a voltage of 800 V being applied between tip 10 and substrate plate 7. The radius of the tip is about 0.5 mm. By switching off the voltage, the drop adhering to the tip is transferred into a vessel including 65 µl of water.

Using spectrophotometry, the dye concentration in the water is subsequently determined to be 4.54×10^{-7} mol/l, corresponding to a volume V = 2.95 nl transferred by the tip. The transfer is conducted 5 times in the same way, with no loss of transferred volume resulting within the relative dosing error of 1.5%.

Example 3

A further example illustrates dosing and complete transfer of liquid drops, using the device of Figure 2.

A drop 8 of a solution of 4-(6-diethylamino-3-diethylimino-3H-xanth-9-yl)-1,3-benzenedisulfonic acid (Kiton Red, concentration: 1×10^{-2} mol/l in water) rests on the ultraphobic surface. The volume $V_3 = (3.00 \pm 0.05) \times 10^{-9}$ liters.

Another drop 9 of a solution of 1,1'-diethyl-4,4'-dicarbocyanine iodide (concentration: 1×10^{-2} mol/l in water) rests on the ultraphobic surface. The volume $V_4 = (3.00 \pm 0.05) \times 10^{-9}$ liters.

Using the tip 10, the drop 8 is picked up as in Example 2. By switching off the voltage, the drop adhering to the tip is deposited in a well 11 of the device. The other drop 9 is picked up with the tip and combined with drop 8 in the well. Subsequently, both drops are picked up with the tip and transferred in accordance with Example 2 into a vessel including 65 µl of water.

The concentrations of the dyes in the water are subsequently determined using spectrophotometry. The transfer is conducted 5 times in the same way, with no loss of the transferred volumes V_3 and V_4 resulting within the relative dosing error of 1.5%.

Example 4

Fig. 3 shows an arrangement for discharging small defined volumes of liquid from a reservoir (cross-sectional drawing). The arrangement consists of an electrode 12 with a round tip (1 mm in diameter) and an annular electrode 13 (inner diameter: 0.5 mm). Both electrodes are provided with an ultrahydrophobic coating, the production of which has been described in Example 1. The arrangement

is immersed in an aqueous solution of 4-(6-diethylamino-3-diethylimino-3H-xanth-9-yl)-1,3-benzenedisulfonic acid (Kiton Red, concentration: 1×10^{-2} mol/l in water) as shown in Fig. 3. When applying a voltage of 900 V between the annulus 13 and the electrode 12, a liquid drop 15 is discharged from the reservoir 14 and remains adhered to the electrode 12. The drop can be transferred to another vessel by lateral tilting and switching off the electric field. The volume of drop 15 is determined by measuring the fluorescence intensity of the dye in a known volume of water. After 30 discharge repetitions, a volume of $(65.0 \pm 0.2) \times 10^{-9}$ liters is obtained.

Example 5

An arrangement as in Fig. 4 can be used instead of the annular electrode 13 of the device in Fig. 3. Therein, three round electrodes 16 (1 mm in diameter) are provided with an ultrahydrophobic coating, the production of which has been described in Example 1. As described in Fig. 4, the electrodes 16 are arranged to form a nearly triangular gap M which assumes the same function as the annular electrode 13 in Fig. 3. Using this arrangement, a liquid drop is discharged from a reservoir as in Example 1. With 30 discharge repetitions, a volume of $(50.0 \pm 0.3) \times 10^{-12}$ liters is obtained.

Similarly, other structures (round, square gaps or gaps of any shape in cross-sectional or top view) can be used for dosing instead of the annulus 13 in Fig. 3. Structures which can be generated using familiar microstructuring techniques (e.g. light, X-ray or electron lithographic techniques) are particularly suited to this end, because small volumes to be dosed require correspondingly small structures.

Claims:

1. A method of moving or dosing liquid drops on a microscopic scale, characterized in that the liquid drops (8, 9) are moved on a support (7) having an ultraphobic surface, using an inhomogeneous electric field, preferably an inhomogeneous electric field between said support (7) and a manipulator (10).

2. The method according to claim 1, characterized in that an electrically charged tip or wire, particularly a tip or wire having an ultraphobic surface is used as manipulator (10).

3. The method according to claim 1 or 2, characterized in that a voltage of from 100 to 1000 volts, preferably from 400 to 600 volts, is applied between manipulator (10) and support (7) in order to generate the electric field.

4. A device for dosing liquid drops, which device has at least one support (7) having an ultraphobic surface, optionally at least one liquid reservoir, an electrically chargeable manipulator (10), and a means for generating an inhomogeneous electric field.

5. The device according to claim 4, characterized in that the manipulator (10) has a tip with an ultraphobic surface, particularly with a diameter of from 0.01 to 1 mm.

6. The device according to any of claims 1 to 5, characterized in that the ultraphobic surface has a surface topography where the spatial frequency f of the individual Fourier components and their amplitudes a(f) expressed by the integral of the function $S(\log f) = a(f) \times f$ calculated between the integration limits $\log(f_1/\mu m^{-1}) = -3$ and $\log(f_1/\mu m^{-1}) = 3$ is at least 0.5 and consists of ultraphobic polymers or durably ultraphobic materials.

7. The device according to any of claims 1 to 6, characterized in that the ultraphobic surface is a structured aluminum surface coated with an ultraphobic material.

8. The device according to any of claims 1 to 6, characterized in that the ultraphobic surface is an aluminum surface treated with steam and coated with an ultraphobic material.

9. The device according to any of claims 1 to 6, characterized in that the ultraphobic surface is a surface which is coated with $Ni(OH)_2$ particles and covered with an ultraphobic material.

10. The device according to any of claims 1 to 6, characterized in that the ultraphobic surface is a sandblasted surface covered with an ultraphobic material.

11. The device according to any of claims 1 to 6, characterized in that the ultraphobic surface is a tungsten carbide surface structured by a laser and covered with an ultraphobic material.

12. Use of the device according to any of claims 4 to 11 in the dosage of liquids on a microscopic scale, especially in a range of from 10^{-6} to 10^{-12} liters, preferably from 10^{-9} to 10^{-6} liters.

13. Use of the device according to any of claims 4 to 11 in biochemical or chemical processes, preferably in PCR, ELISA and/or in the determination of enzyme activity.

Abstract:

The invention relates to a method and a device which serves for moving and dosing amounts of liquid on a microscopic scale with a volume of especially 10^{-12} to 10^{-6} liters by means of an inhomogeneous electric field using a support having an ultraphobic surface.

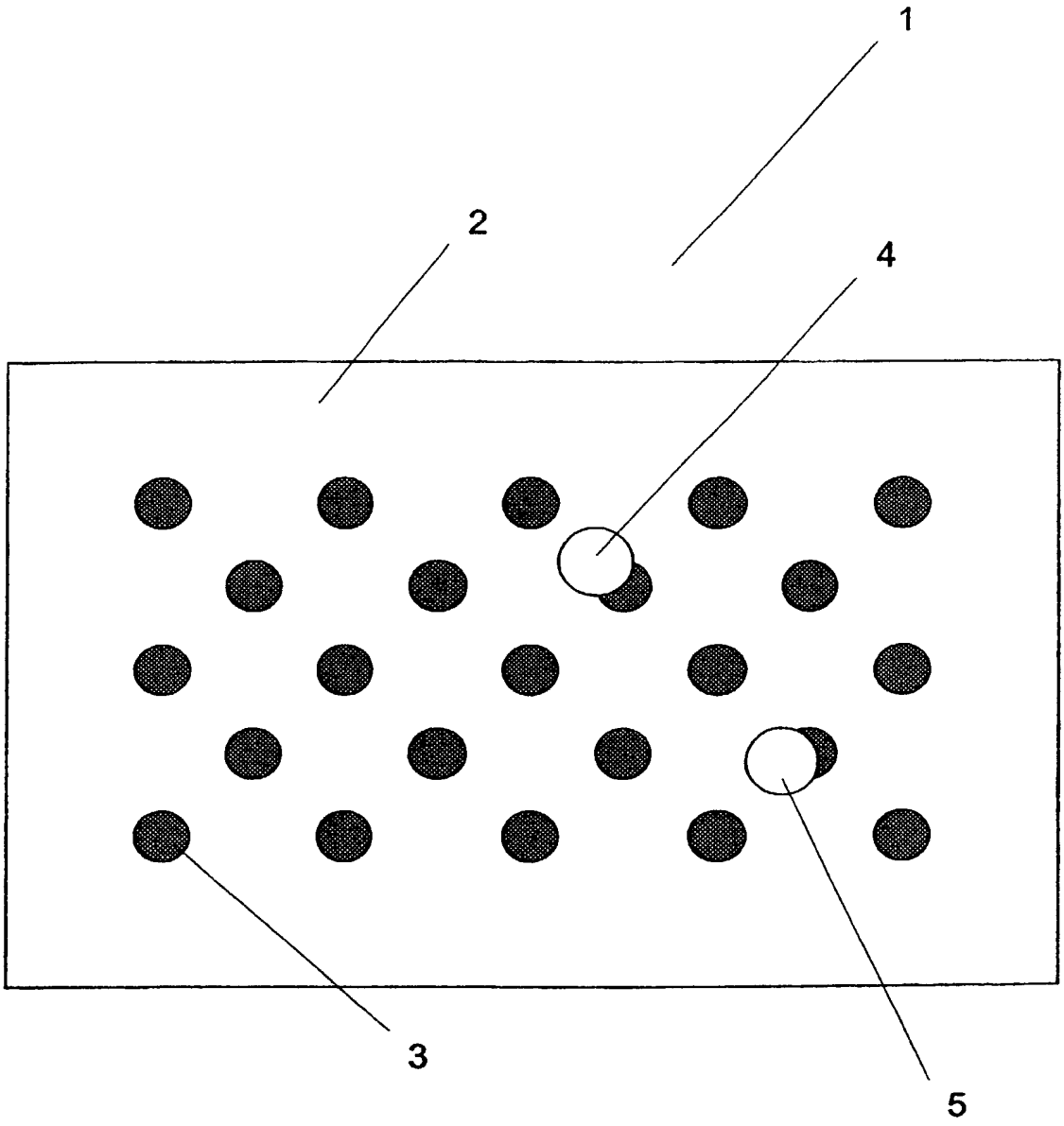

Figure 1

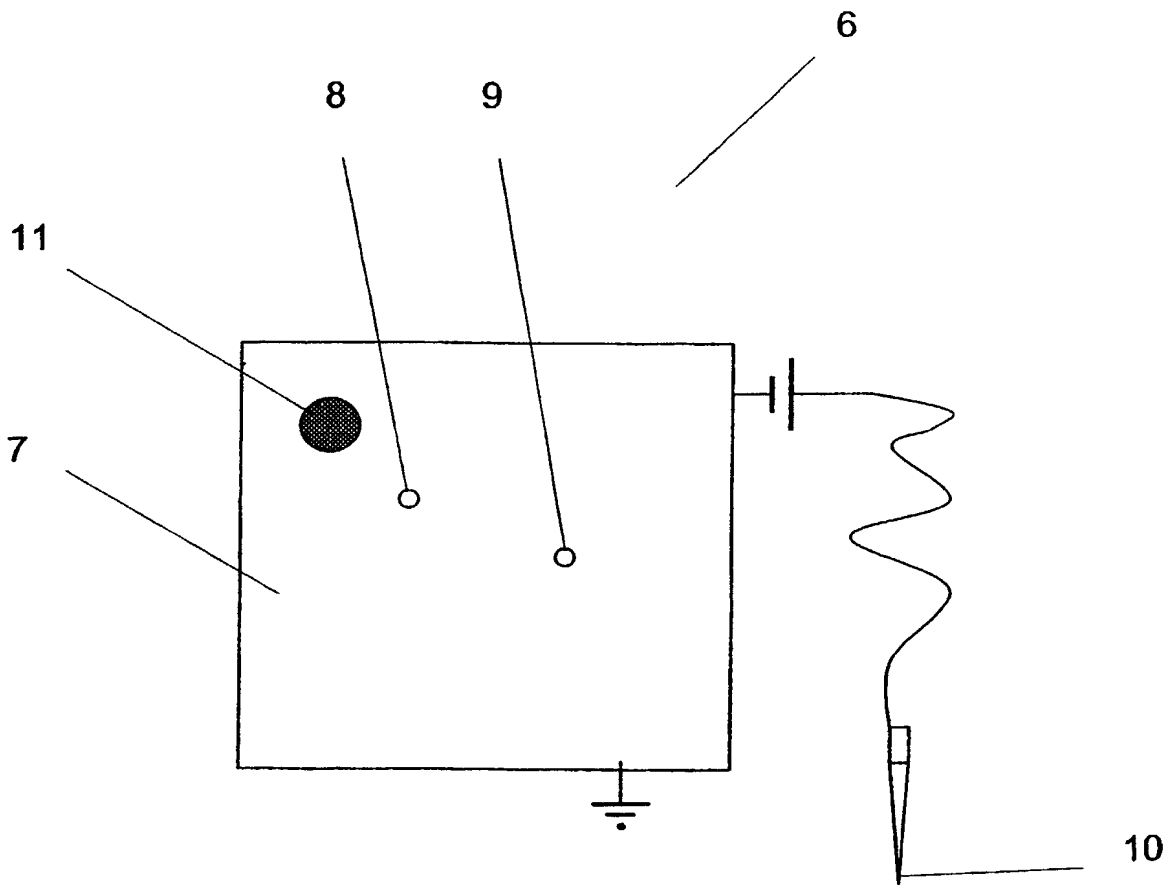

Figure 2

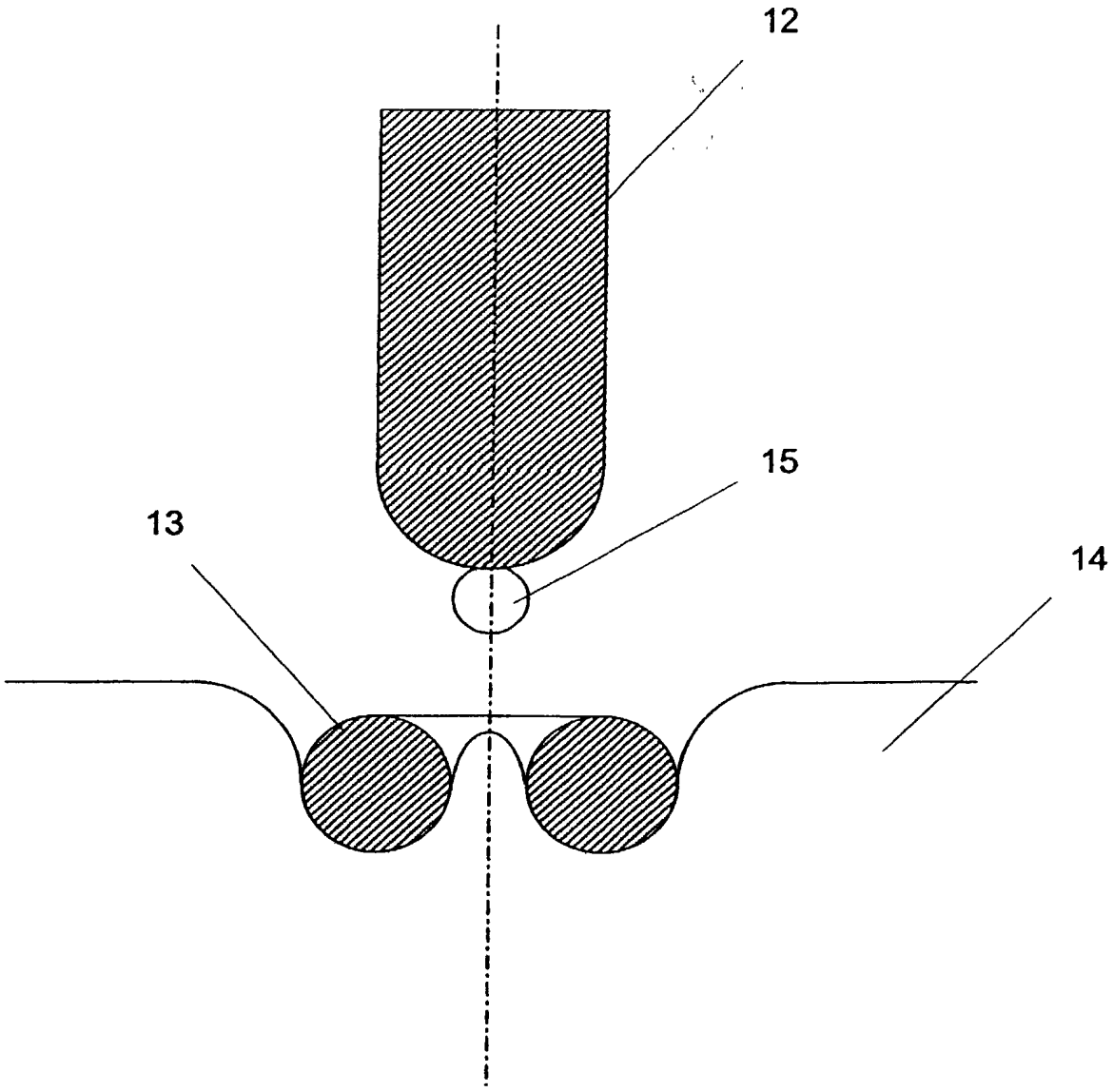

Figure 3

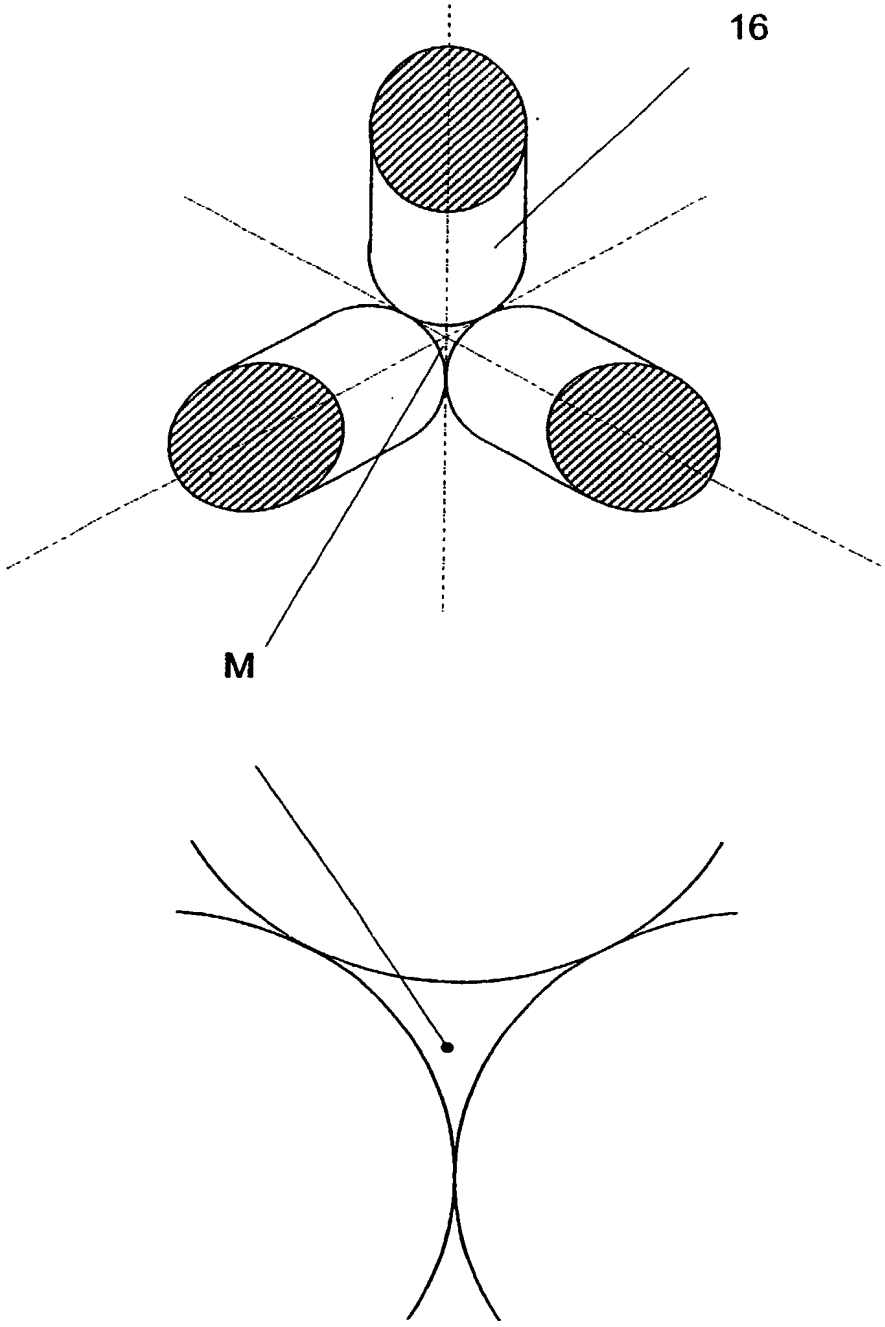

Figure 4

Docket No.: _____

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Title: **METHOD AND DEVICE FOR MOVING AND PLACING LIQUID DROPS IN A CONTROLLED MANNER**

the specification of which

(check one)

☐ is attached hereto.

☒ was filed on _____ as United States Application No. **10/089,933**

or PCT

International Application Number **PCT/EP00/09272** filed on **22.09.2000**

and was amended on (if applicable) _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International Application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)

(Number)	(Country)	(Day/Month/Year Filed)	Priority Not Claimed
199 47 788.4	**DE**	**05.10.1999**	☐
			☐
			☐
			☐

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below:

_____ (Application Serial No.) _____ (Filing Date)

_____ (Application Serial No.) _____ (Filing Date)

_____ (Application Serial No.: _____ (Filing Date)

I hereby claim the benefit under 35 U.S.C. Section 120 of any United States application(s), or Section 365(c) of any PCT International Application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International Application in the manner provided by the first paragraph of 35 U.S.C. Section 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C.F.R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

_____ (Application Serial No.) _____ (Filing Date) _____ (Status) (patented, pending, abandoned)

_____ (Application Serial No.) (Filing Date) _____ (Status) (patented, pending, abandoned)

_____ (Application Serial No.) _____ (Filing Date) _____ (Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. (list name and registration number)

All attorneys listed under Customer No.: 2512

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Fifth inventor's signature: DATE

Residence address:

Citizenship

Post Office Address

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